

REMARKS

Claims 6, 12-17 and 19 are canceled. Applicant reserves the right to pursue the canceled subject matter in one or more continuing applications. No claim has been amended.

Upon entry of this amendment claims 1-5, 7-11, 18, and 20-22 will be pending.

Rejections Under 35 USC §103(a) Obviousness

Claims 1, 3-5, 7 and 9-11 have been rejected as unpatentable over WO 98/33379 (Lerner) in view of U.S. Pat. No. 6,037,481 (Zucchetti). The rejection argues that because Lerner teaches the administration of NOS inhibitors, e.g., L-NAME, "for the treatment of unwanted conditions of skin associated with aging" and Zucchetti teaches that "wrinkles are an unwanted effect of skin aging", it would have been obvious to one of skill in the art to modify Lerner's method and apply L-NAME to wrinkles. Applicants respectfully traverse this rejection.

Contrary to Examiner's argument, Lerner's teachings are not as broad as teaching the administration of NOS inhibitors generally, and L-NAME in particular, to treat all unwanted conditions of the skin associated with aging. Lerner teaches treating a subset of conditions associated with aging, i.e., those conditions that are characterized by too many or too few melanocytes or keratinocytes. See Lerner page 2, lines 16-25, which provides:

In one aspect the invention features, a method of treating a subject, e.g., a human, for an unwanted epidermal or dermal growth condition. The method includes administering to the subject, a treatment which modulates the level of nitric oxide (NO) in the skin. Conditions characterized by unwanted cells, e.g., melanocytes or keratinocytes, the proliferation of such cells, or a deficiency in apoptosis of such cells, or unwanted pigmentation, are treated by increasing the level of NO in the skin. Conditions characterized by the lack of or by an insufficient number of dermal or epidermal cells, e.g., melanocytes or keratinocytes or a lack of pigmentation, are treated by reducing the level of NO in the skin. (Emphasis added.)

Neither Lerner nor Zucchetti teach or suggest that wrinkles are in any way associated with unwanted proliferation or insufficient number of melanocytes or keratinocytes. Thus, a skilled artisan cannot arrive at the claimed methods from the cited combination of references.

Furthermore, even if Lerner did disclose treating skin conditions generally by modulating NO, a skilled artisan would not have the requisite motivation or reasonable expectation of success to inhibit NO levels to treat wrinkles. Lerner discloses the use of compounds that reduce NO levels, e.g., L-NAME, to treat some disclosed unwanted skin conditions, Lerner also discloses the use of compounds that increase NO levels in the skin to treat other unwanted skin conditions. Wrinkles are not disclosed. Neither Lerner nor Zucchetti, provides any guidance that would lead a person of ordinary skill in the art to decide whether wrinkles are the type of unwanted skin condition that should be treated by decreasing NO levels, or whether wrinkles are the type of unwanted skin condition that should be treated by increasing NO levels. The fact that Zucchetti identifies wrinkles as a skin condition associated with aging in no way makes up for this deficiency.

More specifically, Lerner in no way precludes the administration of compounds that increase NO levels to treat conditions associated with aging. Lerner's disclosure does not limit those conditions treated with NO donors (as opposed to NOS inhibitors) to conditions that are not associated with aging; i.e. nowhere does Lerner suggest that if an unwanted skin condition is associated with aging, then it can only be treated by decreasing NO levels as opposed to increasing NO levels. For this reason, Lerner's disclosure provides no guidance that would lead a person of ordinary skill in the art to decide whether wrinkles are the type of unwanted skin condition that should be treated by decreasing NO levels, or whether wrinkles are the type of unwanted skin condition that should be treated by increasing NO levels.

Zucchetti's disclosure also provides no guidance in this matter. Zucchetti's disclosure that wrinkles are a condition of the skin associated with aging provides no suggestion or motivation for the conclusion that wrinkles are the type of skin condition that can be treated by modulating NO, at all. Even less does Zucchetti provide any guidance, suggestion, or motivation, much less a reasonable expectation of success, for preferentially adapting either of Lerner's methods (increasing or decreasing NO) to the treatment of wrinkles.

In summary, Examiner has not pointed to any teaching or suggestion in either Lerner or Zucchetti that would guide a skilled artisan to identify wrinkles as a condition of the skin to be

treated by either decreasing or increasing NO. Without a suggestion that wrinkles are at least the kind of condition that can be treated by decreasing NO or administering L-NAME, the subject matter of the present claims cannot be rendered obvious by either of these references, alone or in combination.

For the reasons presented above, applicants respectfully request that this rejection be withdrawn.

Claims 2 and 8 stand rejected as allegedly unpatentable over Lerner in view of EP 0755671A1 (Yamaguchi). The rejection argues that Lerner discloses L-NAME for the treatment of sunburn or other exposure to UV light, and Yamaguchi discloses that it is known that exposure to UV rays accelerates the formation of wrinkles. The rejection concludes that the combination of these two teachings render obvious the use of L-NAME for the treatment of wrinkles. Applicants respectfully traverse this rejection.

Again, the rejection attributes to Lerner the overly broad teaching that **all** unwanted conditions of the skin caused by exposure to the sun or UV light can be treated with L-NAME. The rejection combines this overly broad reading of Lerner with a reference disclosing that wrinkles are **one** condition of the skin that can be accelerated by UV light, and the rejection concludes that together these teachings render obvious the treatment wrinkles with L-NAME. Contrary to the Examiner's argument, i.e. Lerner does not teach that all skin conditions accelerated by UV light can be treated with L-NAME.

As noted above, the root of Lerner's teachings regarding L-NAME are that lowering NO levels in the skin decreases the cell death of melanocytes and keratinocytes. See also, e.g., p. 4 lines 1-12. This mechanism does implicate some conditions associated with UV light, such as pigmentation related conditions and sunburn, which are disclosed in Lerner. However, neither Lerner nor Yamaguchi teaches or suggests that decreasing melanocyte or keratinocyte cell death is an appropriate mechanism for the treatment or reduction of wrinkles. Therefore, neither reference alone or in combination provides the reasonable expectation of success that would

motivate a skilled artisan to adapt the L-NAME treatment disclosed by Lerner to the treatment of wrinkles caused by UV light.

The rejection completely ignores the disclosures in Lerner of conditions that are also accelerated by UV radiation, but which Lerner teaches are treated by increasing NO levels (in contrast to the claimed methods, which include administering a NOS inhibitor). For example, Lerner discloses that “conditions characterized by unwanted cells, e.g., melanocytes..., the proliferation of such cells...are treated by increasing the level of NO in the skin,” p.2 lines 19-21 (emphasis added). To illustrate, melanomas are a condition characterized by the unwanted proliferation of melanocytes and are also a condition accelerated by UV light. Under the reasoning of the present Office Action, Lerner, in combination with the knowledge that melanomas are associated with exposure to UV light, makes it obvious that melanomas should be treated by decreasing levels of NO with L-NAME. The conclusion of this analysis, however, flies in the face of Lerner’s explicit teaching that the unwanted proliferation of melanocytes is treated by increasing NO levels, regardless of the fact that unwanted proliferation of melanocytes is associated with UV radiation.

In another example, Lerner discloses that reducing NO levels in the skin, e.g., using L-NAME, is a method for darkening a person’s skin. See, e.g., p.5, lines 17-20 and claim 22. Yet under the logic of the rejection, L-NAME should be a method for treating or reducing darkening of the skin because skin tanning is a condition accelerated by UV light. The logic of the rejection, again, directly contradicts the specific teaching in Lerner that administration of L-NAME is a method of darkening the skin; and that lightening of the skin is accomplished by increasing NO levels, not by decreasing NO levels. p.5 lines 5-8, and claim 21.

For the reasons presented above, the combination of Yamaguchi and Lerner do not render the presently claimed methods obvious and applicants respectfully request this rejection be withdrawn.

Claims 18-22 stand rejected as allegedly unpatentable over Lerner in view of Zucchetti and in further view of Remington’s Pharmaceutical Sciences, 17th ed. (Remington). The

rejection applies Lerner and Zucchetti, as described above, in combination with Remington's teaching that there is a general awareness that labeling instructions are needed to ensure patients understand how to safely and effectively use prescription medications.

Applicants reiterate, for the reasons presented above, that Lerner and Zucchetti do not make obvious the use of L-NAME in a method of treating or reducing wrinkles. Remington does not suggest the use of L-NAME in a method of treating or reducing wrinkles. Without a suggestion or teaching that L-NAME can be used to treat wrinkles, Remington does not supply the required motivation to perform a method that includes supplying instructions for using L-NAME to treat wrinkles.

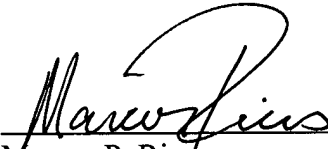
For the reasons presented above applicants respectfully request that this rejection be withdrawn.

Please apply any charges or credits to deposit account 06-1050.

Respectfully submitted,

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